II. REMARKS

Formal Matters

Claims 1-70 are pending after entry of the amendments set forth herein.

Claims 5-12 were examined. Claim 8 was rejected. Claims 5-7 and 9-12 were allowed. Claims 1-4 and 13-57 were withdrawn from consideration.

Claims 5, 7-9, and 12 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claim 5, 7-9 and 12 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: claim 5: page 4, lines 17-18. Accordingly, no new matter is added by these amendments.

New claims 58-70 are added. Support for new claims 58-70 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: claim 58: page 7, lines 3-15; claims 59-61: page 7, lines 11-12; claim 62: page 7, lines 11-14; claim 63: page 8, line 21 to page 9, line 4; page 8, line 29 to page 9, line 2; claim 64: Figure 1; and sequence listing; claims 65 and 66: page 12, lines 11-18; claim 67: Figure 1 and sequence listing; claim 68: page 11, lines 8-12; claims 69 and 70: page 10, lines 2-5. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

PTO 1449/SB-08A form

A Request for Continued Examination is being filed so that the references provided along with the SB-08A forms filed on January 2, 2003, February 6, 2003, and February 10, 2003 can be considered and made of record in the instant application. Applicants respectfully request that the Examiner initial and return the SB-08A forms submitted with the Information Disclosure Statements filed on January 2, 2003, February 6, 2003, and February 10, 2003 in this application, thereby indicating that the references cited therein have been reviewed and made of record.

Withdrawal of previous rejections

Applicants note with gratitude that the following rejections, raised in the March 27, 2002 Office Action, were withdrawn: (1) rejection of claim 8 under 35 U.S.C.§112, second paragraph; (2) rejection of claims 5 and 7-11 under 35 U.S.C.§112, first paragraph; (3) rejection of claims 5, 6, and 7-11 under

35 U.S.C.§102(e); (4) rejection of claims 5, 6, and 8-11 under 35 U.S.C.§102(a); and (5) rejection of claims 5 and 7-11 under 35 U.S.C.§102(b).

Allowable subject matter

Applicants note with gratitude that claims 5-7 and 9-12 are deemed allowable.

Claim objection

Claim 6 was objected to because SEQ ID NO:11 is disclosed in the specification to encode GST-4β, but is currently recited in claim 6 as encoding GST-4α.

Applicants respectfully note that SEQ ID NO:11 comprises a human GST-4α coding sequence. Specification, page 11, lines 23-24. Accordingly, SEQ ID NO:11 is properly included in claim 6.

Rejection under 35 U.S.C.§112, first paragraph

Claim 8 was rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement.

The Office Action stated that the specification, while being enabling for isolated DNA sequences encoding SEQ ID NO:8 and homologs thereof of at least 85% identity to SEQ ID NO:8, does not reasonably provide enablement for isolated DNA sequences that hybridize to DNA sequences encoding homologs of SEQ ID NO:8 at 50°C or higher in a solution of 15 mM NaCl and 1.5 mM Na citrate or complementary sequences thereof. Applicants respectfully traverse the rejection.

The Office Action stated that the specification fails to provide any support about the structural requirements of DNA sequences that can hybridize to those encoding the above-mentioned homologs of SEQ ID NO:8 with capability of encoding GST. The Office Action stated that no information about the critical residues which must be present in the claimed DNA sequences in order to encode a product with GST4α activity can be found in the specification. The Office Action stated that one of skill in the art has to go through the burden of undue experimentation in order to make the claimed DNA sequences and as such the claim goes beyond the scope of the disclosure.

As a preliminary matter, without acquiescing to this rejection and in the interest of expediting prosecution, claim 8 has been amended to recite "an isolated nucleic acid that hybridizes at 50°C or higher in a solution of 15 mM NaCl and 1.5 mM sodium citrate to a nucleic acid comprising a nucleotide sequence as set forth in SEQ ID NO:08 or a complementary sequence thereof, wherein said nucleic acid encodes a glycosyl sulfotransferase." The arguments presented herein apply to the claim 8 before amendment and to the extent that this rejection might be applied to claim 8 as amended.

The law regarding enablement of inventions is clear: "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."[1]

To aid in determinations of enablement, courts have identified eight factors for consideration: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance provided; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability or unpredictability of the art; and (h) the breadth of the claims.[2]

Applicants respectfully submit that the specification, coupled with the information known in the art, would enable one of skill in the art to use the invention without undue experimentation. Relevant enablement factors are discussed in detail below.

(a) the quantity of experimentation necessary:

The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.[3]

As the court explained[4]:

> "[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the

[1] *United States v. Telectronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997); *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

[2] *Ex Parte Forman.*, 230 USPQ 546, 547 (Bd.Pat.App & Interf. 1986); and, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

[3] See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

[4] *In re Wands* 8 USPQ 2d at 1404

direction in which the experimentation should proceed."

Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, the court concluded that extensive screening experiments, while being voluminous, were not undue in view of the art which routinely performs such long experiments.[5]

Claim 8 as amended recites a nucleic acid that hybridizes under the recited stringent hybridization conditions to a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:08; and recites that the nucleic acid encodes a glycosyl sulfotransferase. The only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to determine which sequences hybridize under stringent hybridization conditions to a nucleic acid comprising the sequence set forth in SEQ ID NO:08 and encode glycosyl sulfotransferase. Nucleic acids that hybridize under stringent hybridization conditions to a given nucleic acid is identified through routine experimentation, employing nothing more than standard nucleic acid hybridization techniques. Polypeptides that are glycosyl sulfotransferases are identified through routine experimentation, typically employing nothing more than performing the same assay disclosed in the specification on a variety of polypeptides made by routine expression, using recombinant DNA techniques, of the identified nucleic acids. In other words, the only experimentation that may be required to enable the claimed invention are those experiments to determine the presence of a certain activity, and since this only requires a routine hybridization technique, followed by a routine assay on polypeptides to determine the glycosyl sulfotransferase activity, no undue experimentation is necessary.

b) the amount of direction or guidance provided

The instant specification provides guidance for identifying a nucleic acid that hybridizes, under the recited stringent hybridization conditions, to a nucleic acid comprising the sequence set forth in SEQ ID NO:08; and how to determine whether a polypeptide encoded by the nucleic acid is a glycosyl sulfotransferase.

Claim 8 as amended recites a nucleic acid that hybridizes, under the recited stringent hybridization conditions, to a nucleic acid comprising a sequence as set forth in SEQ ID NO:08. The specification discusses how to identify nucleic acids that hybridize under stringent hybridization conditions, as recited in claim 8, to a given nucleic acid, e.g., SEQ ID NO:08. Specification, page 19, lines 3-16. Such methods are well known in the art, and have been standard laboratory practice for over 15 years.

Once a nucleic acid is identified, it is well within the skill level of those of ordinary skill in the art to produce a polypeptide encoded by the nucleic acid. The instant specification describes in detail how to express a given nucleic acid, and to produce a polypeptide encoded by the nucleic acid. Specification, page 15, line 3 to page 18, line 15. Again, polypeptides are produced using standard laboratory practices that have been in use for at least 15 years.

Claim 8 recites that the nucleic acid encodes a glycosyl sulfotransferase. The instant specification discusses glycosyl sulfotransferase activity, and states that, as is well known in the art, a glycosyl sulfotransferase catalyzes the transfer of a sulfate group from a donor to an acceptor ligand. Specification, page 7, lines 3-15. The specification discusses how to determine whether a polypeptide exhibits glycosyl sulfotransferase activity. Specification, page 27, lines11-29. Such assays are well known in the art.

Thus, given the guidance in the specification, one of ordinary skill in the art could readily identify nucleic acids that hybridize under the recited stringent hybridization conditions to SEQ ID NO:08; and could readily determine whether a polypeptide encoded by the nucleic acid was a glycosyl sulfotransferase.

(c) the presence or absence of working examples:

Compliance with the enablement requirement under 35 U.S.C. §112, first paragraph does not require or mandate that a specific example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.[6] Furthermore, "Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad

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[5] *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)
[6] In re Borkowski, 164 USPQ at 645.

terminology or illustrative examples."[7]

(f) the relative skill of those in the art:

The relevant ordinarily skilled artisan is generally a skilled laboratory technician with experience in molecular biology and/or a scientist with the equivalent of a doctoral degree in molecular biology techniques. Furthermore, as discussed above, the techniques required to make and use a nucleic acid as recited in claim 8 are standard laboratory techniques that have been in use for years. As such, the skill level of those developing and using methods for manipulating DNA and performing enzymatic activity assays is high.

(g) the predictability or unpredictability of the art

In making this rejection, the Examiner pointed to the "unpredictability of prior art as to how to construct such DNA sequences such that they encode a product with a GST4 alpha function." Office Action, page 4.

However, as discussed above, in view of the high level of skill of those of ordinary skill in the art, generation of nucleic acids that hybridize with a given nucleic acid is not unpredictable; expressing a given nucleic acid such that an encoded polypeptide is produced is not unpredictable; and determination of whether a given polypeptide has glycosyl sulfotransferase activity is readily accomplished through routine experimentation. Accordingly, generation of a nucleic acid as recited in claim 8 is not unpredictable.

The court has very clearly explained[8]:

> "To require such a complete disclosure would apparently necessitate a patent application or applications with thousands of catalysts....More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid literal infringement of such claims by merely finding another analogous catalyst complex which could be used ...."

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[7] *In re Robins* 166 USPQ 552 at 555 (CCPA 1970).
[8] *In re Angstadt*, 190 USPQ at 218.

Claim 8 recites a nucleic acid that hybridizes under the recited conditions to a nucleic acid having a sequence as set forth in SEQ ID NO:08 and that encodes a glycosyl sulfotransferase. Since one of skill in the art would recognize that a reasonable correlation exists between the hybridization under stringent conditions to a nucleic acid comprising the sequence set forth in SEQ ID NO:08 and encoding a glycosyl sulfotransferase, and since every species in a genus does not have to be tested for a genus to be enabled, extensive disclosure or guidance of the active species of a genus does not have to be provided for a genus of this scope to be enabled.

(h) the breadth of the claims

The claims of the instant application encompass sequences that encode a glycosyl sulfotransferase. In other words, in order to fall within a claim, a sequence must encode a glycosyl sulfotransferase. *Thus, the claim language excludes nucleic acids that do not encode a glycosyl sulfotransferase.*

In sum, the amount of experimentation required to identify nucleic acids that hybridize under the recited stringent hybridization conditions to a nucleic acid comprising the sequence set forth in SEQ ID NO:08 and that encode a glycosyl sulfotransferase would not be undue because a) the specification provides guidance as to how to identify nucleic acids that hybridize under stringent hybridization conditions to a given nucleic acid, and the techniques for doing so were well known in the art; b) the specification provides guidance as to how to produce a polypeptide encoded by a nucleic acid so identified, and the techniques for doing so were well known in the art; c) the specification provides guidance as to how to determine whether a given polypeptide is a glycosyl sulfotransferase, and the techniques for doing so were well known in the art; and d) one of skill in the art would be able to perform the experiments as a matter of routine to make the nucleic acids as claimed.

The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

Applicants submit that the rejection of claim 8 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(e)

Claim 8 was rejected under 35 U.S.C.§102(e) as allegedly anticipated by Bistrup et al. (U.S. Patent No. 6,295,192).

The Office Action stated that Bistrup teaches a DNA sequence encoding GST that has 63.3% local similarity to SEQ ID NO:04 of the instant application. Applicants respectfully traverse the rejection.

Without acquiescing to the rejection, and solely in the interest of expediting prosecution, claim 8 as amended recites an isolated nucleic acid that hybridizes at 50°C or higher in a solution of 15 mM NaCl and 1.5 mM sodium citrate to a nucleic acid comprising a nucleotide sequence as set forth in SEQ ID NO:08.

Applicants submit that the rejection of claim 8 under 35 U.S.C. §102(e) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Species election

Applicants respectfully request that the examiner consider the non-elected species.

Rejoinder

Applicants respectfully request rejoinder of method claims to the extent that they incorporate all the limitations of an allowed claim, as provided for under MPEP §821.04.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL138.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Apr. 10, 2003

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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